

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

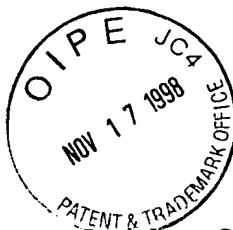
In re Application of:

Ross, et al.

Serial No.: 09/134,419

Group Art Unit: 1614

Filed: August 14, 1998

For: **Heterocyclic Esters or Amides for Vision and Memory Disorders**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENTAssistant Commissioner for Patents
Washington, D.C. 20231

NOV 18 1998

Sir:

Pursuant to Applicants' duty of disclosure under 37 C.F.R. §§ 1.56 and 1.97-1.99, the documents listed on the attached Form PTO-1449 are being brought to the attention of the Examiner in charge of the captioned application. No fee is required for this submission because it is submitted within three months from the filing date or before a First Office Action on the merits has been mailed by the U.S. Patent and Trademark Office (USPTO).

A completed Form PTO-1449 is attached hereto. Copies of the cited references are concurrently filed with the Information Disclosure Statement in U.S. Patent Application No. 09/134,422, pursuant to agreement with Examiner Zohreh Fay, Art Group 1614. If additional copies of the references cited herein are required, kindly telephone the undersigned attorney. The Examiner is respectfully requested to cite the documents listed on the attached Form PTO-1449 in the next Office Action. In so doing, the Examiner

PATENT

Attorney Docket No. 23138S

Serial No.: 09/134,419

is respectfully requested to initial in the space adjacent to the listing of each document on the Form PTO-1449, and return a copy of the initialed Form PTO-1449 with the next communication to Applicants, to confirm that these documents have been considered by the Examiner and made of record in this application.

If the Examiner has any questions or wishes to discuss this application, kindly telephone the undersigned attorney.

Respectfully submitted,

NATH & ASSOCIATES

Date: November 16, 1998



Gary M. Nath
Reg. No. 26,965
Suet M. Chong
Reg. No. 38,104
Lee C. Heiman
Reg. No. 41,827

NATH & ASSOCIATES

1030 15th Street, N.W.
6th Floor

Washington, D.C. 20005

Tel: (202) 775-8383

Fax: (202) 775-8396

GMN:SMC:LCH:dhy

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419

Applicant

Ross, et al.

Filing Date

August 14, 1998

Group Art Unit

1614

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	AA	5,703,088	12/30/97	Sharpe et al.			6/4/92
	AB	5,631,017	5/20/97	Sharpe et al.			3/26/93
	AC	5,614,547	3/25/97	Hamilton et al.			6/7/95
	AD	5,543,423	8/6/96	Zelle et al.			1/23/95

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub-Class	Trans-lation
	AE	DE4015255	11/14/91	Germany			No
	AF	DE3931051	3/29/90	Germany			No
	AG	DE3508251	9/11/86	Germany			No
	AH	EP-652229	5/10/95	EPO			Yes
	AI	EP-572365	12/1/93	EPO			Yes
	AJ	EP-468339	1/29/92	EPO			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AK		Ando, Takao et al., "Formation of Crossed Phenazine from the Reaction between Tetra-p-anisyl- and Tetra-p-tolyl-hydrazines in Liquid Sulphur Dioxide," Chem. Comm., S. Chem. Comm., 1975, 989.
	AL		Andrus, Merrit B., "Structure-based design of an acyclic ligand that bridges FKBP12 and calcineurin," J. Am. Chem. Soc., 1993, 115(2), 10420-1.
	AM		Armistead, D.M. et al., "Design, synthesis and structure of non-macrocyclic inhibitors of FKBP12, the major binding protein for the immunosuppressant FK506," Acta Crystallogr. 1995, D51(4), 522-8.
	AN		Askin, D. et al., "Chemistry of FK-506: benzilic acid rearrangement of the tricarbonyl system," Tetrahedron Lett., 1989, 30(6), 671-4.
	AO		Askin, D. et al., "Efficient Degradation of FK-506 to a versatile synthetic intermediate," J. Org. Chem., 1990, 55(20), 5451-4.
	AP		Baader, Ekkehard et al., "Inhibition of prolyl 4-hydroxylase by oxalyl amino acid derivatives in vitro, in isolated microsomes and in embryonic chicken tissues," Biochem. J., 1994, 300(2), 525-30.

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.

Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATION

Attorney Docket 23138S	Serial Number 09/134,419
Applicant Ross, et al.	
Filing Date August 14, 1998	Group Art Unit 1614

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	BA	5,516,797	5/14/96	Armistead et al.			4/11/94
	BB	5,447,915	9/5/95	Schreiber et al.			8/28/92
	BC	5,424,454	6/13/95	Burbaum, B.W. et al.			5/26/94
	BD	5,414,083	5/9/95	Hackl et al.			1/24/94

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub-Class	Translation
	BE	EP-419049	3/27/91	EPO			Yes
	BF	EP-405994	1/2/91	EPO			Yes
	BG	EP-378318	7/18/90	EPO			Yes
	BH	EP-352000	1/24/90	EPO			Yes
	BI	EP-333174	9/20/89	EPO			Yes
	BJ	EP-260118	3/16/88	EPO			Yes
	BK	EP-196841	10/8/86	EPO			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	BL		Baumann, K. et al., "Synthesis and oxidative cleavage of the major equilibrium products of ascomycin and Fk 506," Tetrahedron Lett., 1995, 26(13), 2231-4.
	BM		Bender, D., et al., "Periodate oxidation of α -keto γ -lactams. Enol oxidation and β -lactam formation. Mechanism of periodate hydroxylation reactions," J. Org. Chem., 1978, 43(17), 3354-62.
	BN		Birkenshaw, T.N. et al., "Synthetic FKBP12 Ligands. Design and Synthesis of Pyranose Replacements," Bioorganic & Medicinal Chemistry Letters, (1994) 4:21, 2501-2506.
	BO		Boulmedais, Ali et al., "Stereochemistry of Electrochemical Reduction of Optically Active α -ketoamides. II. Electoreduction of benzoylformamides derived from S-(-)-proline," Bull. Soc. Chim. Fr., 1989, (2), 185-91. (French)
	BP		Cameron, Andrew et al., "Immunophilin FK506 binding protein associated with inositol 1,4,5-triphosphate receptor modulates calcium flux," Proc. Natl. Acad. Sci. USA, 1995, 92, 1784-1788.
	BQ		Caufield, Craig E. and Musser, John H., "Macrocyclic Immunomodulators," Annual Reports in Medicinal Chemistry, Johns (Ed.), Academic Press, Chapter 21, 195-204, 1989.

Examiner

Date Considered:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.

Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419Applicant
Ross, et al.Filing Date
August 14, 1998Group Art Unit
1614

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	CA	5,359,138	10/25/94	Takeuchi et al.			6/29/92
	CB	5,330,993	7/19/94	Armistead et al.			7/2/91

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub-Class	Translation
	CC	EP--88350	9/14/83	EPO			Yes
	CD	EP--73143	3/2/83	EPO			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	CE	Caffrey, M.V. et al., "Synthesis and Evaluation of Dual Domain Macrocyclic FKBP12 Ligands," <u>Bioorganic & Medicinal Chemistry Letters</u> , (1994) 4:21, 2507-2510.
	CF	Chakraborty, TK et al., "Design and Synthesis of a rapamycin-based high affinity binding FKBP12 ligand," <u>Chem. Biol.</u> , 1995, 2(3), 157-61.
	CG	Chakaraborty, Tushar K., "Studies towards the development of cyclic peptide-based analogs of macrolide immunosuppressants," <u>Pure Appl. Chem.</u> , 1996, 68(3), 565-568.
	CH	Coleman, R., and Danishefsky, S., "Degradation and manipulations of the immunosuppressant FK506: preparation of potential synthetic intermediates," <u>Heterocycles</u> , 1989, 28(1), 157-61.
	CJ	Colombo, L. et al., "Enantioselective synthesis of secondary alcohols in the presence of chiral ligands," <u>Tetrahedron</u> , 1982, 38(17), 2725-7.
	CK	Cunliffe, C. Jane et al., "Novel inhibitors of prolyl 4-hydroxylase. 3. Inhibition by the substrate analog N-oxalglycine and its derivatives," <u>J. Med. Chem.</u> , 1992, 35(14), 2652-8.
	CL	Cushman, D.W. et al., "Design of potent competitive inhibitors of angiotensin-converting enzyme. Carboxyalkanoyl and mercaptoalkanoyl amino acids," <u>Biochemistry</u> , 1977, 16(25), 5484-91.
	CM	Dawson, Ted M. et al., "Immunosuppressant FK506 enhances phosphorylation of nitric oxide synthase and protects against glutamate neurotoxicity," <u>Proc. Natl. Acad. Sci. USA</u> , 1993, 90, 9808-12.
	CN	Dawson, T.M. et al., "The immunophilins, FK506 binding and cyclophilin, are discretely localized in the brain: relationship to calcineurin," <u>Neuroscience</u> , 1994, 62(2), 569-80.

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.
 Draw line through citation if not in conformance and not considered.
 Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419

Applicant

Ross, et al.

Filing Date
August 14, 1998Group Art Unit
1614**U.S. PATENT DOCUMENTS**

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	DA	5,319,098	6/7/94	Burbaum, B.W. et al.			5/26/94
	DB	5,294,603	3/15/94	Rinehart, K.L.			2/18/92

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub-Class	Translation
	DC	EP--50800	5/5/82	EPO			Yes
	DD	EP--48159	3/24/82	EPO			Yes
	DE	EP--12401	6/25/80	EPO			Yes
	DF	GB2247456	3/4/92	United Kingdom			Yes
	DG	JP05178824	7/20/93	Japan			No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	DG		Effenberger F. et al., "Diastereoselective addition of benzenesulfonyl chloride to 1-acryloylproline esters," Chemical Abstracts, 1989, 110:154846h.
	DH		Egbertson, M. and Danishefsky, S., "A synthetic route to the tricarbonyl region of FK-506," J. Org. Chem., 1989, 54(1), 11-12.
	DI		Feutren, Gilles, "The Optimal use of Cyclosporin A in Autoimmune Diseases," J. of Autoimmunity, 1992, 5, 183-95.
	DJ		Finberg, Robert W. et al., "Prevention of HIV-1 Infection and Preservation of CD4 Function by the Binding of CPFs to gp120," Science, 1990, 249, 287-91.
	DK		Fisher, Matthew et al., "On the remarkable propensity for carbon-carbon bond cleavage reactions in the C(8)-C(10) region of FK-506," J. Org. Chem., 1991, 56(8), 2900-7.
	DL		Fry, Lionel, "Psoriasis: Immunopathology and Long-term treatment with Cyclosporin," J. of Autoimmunity, 1992, 5, 277-83.

Examiner

Date Considered:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.

Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419Applicant
Ross, et al.Filing Date
August 14, 1998Group Art Unit
1614**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Sub-Class	Filing Date
EA	5,252,579	10/12/93	Skotnicki et al.			2/16/93
EB	5,147,877	9/15/92	Goulet			9/12/91

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Sub-Class	Translation
EC	JP04149166	5/22/92	Japan		No
ED	WO9824805	6/11/98	PCT		Yes
EE	WO9820893	5/22/98	PCT		Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

EL	Furber, Mark, "FKBP-12-ligand-calceineurin interactions: analogs of SBL506," J. Am. Chem. Soc., 1995, 117(27), 7267-8.
EG	Furber, M. et al., "Studies relating to the immunosuppressive activity of FK506," Tetrahedron Lett., 1993, 34(8), 1351-4.
EH	Goodfellow, Val S. et al., "p-Nitrophenyl 3-diazopyruvate and diazopyruvamide, a New Family of Photoactivatable Cross-Linking Bioprobes," Biochemistry, 28(15), 6346-60.
EI	Goulet, Mark T., and Boger, Joshua, "Degradative studies on the tricarbonyl containing macrolide rapamycin," Tetrahedron Lett., 1990, 31(34), 4845-8.
EJ	Goulet, Mark T. and Boger, Joshua, "Degradative studies on the tricarbonyl containing macrolide rapamycin," Tetrahedron Lett., 1991, 32(45), 6454.
EP	Haeusler, Johannes and Schmidt, Ulrich, "Amino acids and peptides. IX. Pyruvyl amino acids," Chem. Ber., 1974, 107(1), 145-51. (German)
EL	Harding, M.W., et al., "A receptor for the immunosuppressant FK506 is a cis-trans peptidyl-prolyl isomerase," Nature Lett., 1989, 341, 758-60.
EM	Hauske, J.R. et al. "Design and Synthesis of Novel FKBP Inhibitors," J. of Medicinal Chemistry, (1992) 35, 4284-4296.
EN	Hauske, James R. et al., "Investigation of the effects of synthetic, non-cytotoxic immunophilin inhibitors on MDR," Bioorg. Med. Chem. Lett., 1994, 4(17), 2097-102.
EO	Hayward, C.M. et al., "Total Synthesis of rapamycin via a novel titanium-mediated aldol macrocyclization reaction," J. Am. Chem. Soc., 1993, 115(20), 9345-6.
EP	Hayward, C.M. et al., "An application of the Suarez reaction to the regiospecific synthesis of the C ₂₈ -C ₄₂ segment of rapamycin," 3989-92.

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.

Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419

Applicant

Ross, et al.

Filing Date
August 14, 1998Group Art Unit
1614**U.S. PATENT DOCUMENTS**

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	FA	4,818,749	4/4/89	Gold, E.H. et al.			4/4/89
	FB	4,808,573	2/28/89	Gold, E.H. et al.			2/28/89

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub-Class	Translation
	FC	WO9820892	5/22/98	PCT			Yes
	FD	WO9820891	5/22/98	PCT			Yes
	FE	WO9636630	11/21/96	PCT			Yes
	FF	WO9633187	10/24/96	PCT			Yes
	FG	WO9633184	10/24/96	PCT			Yes
	FH	WO9617816	6/13/96	PCT			Yes
	FI	WO9615101	5/23/96	PCT			Yes
	FJ	WO9606097	2/29/96	PCT			Yes
	FK	WO9603318	10/24/96	PCT			Yes
	FL	WO9535367	12/28/95	PCT			Yes
	FM	WO9535308	12/28/95	PCT			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	FN		Holt, D.A. et al., "Design, Synthesis, and Kinetic Evaluation of High-Affinity FKBP Ligands and the X-ray Crystal Structures of Their Complexes with FKBP12," <u>J. Am. Chem. Soc.</u> , (1993) 115, 9925-9938.
	FO		Holt, D.A. et al., "Structure-Activity Studies of Nonmacrocylic Rapamycin Derivatives," <u>Bioorganic & Medicinal Chemistry Letter</u> , (1993) 3:10, 1977-1980.
	FP		Holt, D.A. et al., "Structure-Activity Studies of Synthetic FKBP Ligands as Peptidyl-prolyl Isomers Inhibitors," <u>Bioorganic & Medicinal Chemistry Letters</u> , (1994) 4:2, 315-320.
	FQ		Hearn, Walter R., and Worthington, Robert E., "L-Proline-N-oxalic anhydride," <u>J. Org. Chem.</u> , 1967, 32(12), 4072-4.
	FR		Iwabuchi, T. et al., "Effects of immunosuppressive peptidyl-prolyl cis-trans isomerase (PPIase inhibitors, cyclosporin A, FK506, ascomycin and rapamycin, on hair growth initiation in mouse: immunosuppression is not required for hair growth," <u>J. of Dermatol. Sci.</u> , (1995) 9:1, 64-69.
	FS		Jiang, H. et al., "Induction of anagen in telogen mouse skin by topical application of FK506, a potent immunosuppressant," <u>J. Invest. Dermatol.</u> , (1995) 104:4, 523-525.
	FT		Jones, T. et al., "Chemistry of tricarbonyl hemiketals and application of Evans technology to the total synthesis of the immunosuppressant (-)-FK-506," <u>J. Am. Chem. Soc.</u> , 1990, 112(8), 2998-3017.
	FU		Jones, A. et al., "A formal synthesis of FK-506. Exploration of some alternatives to macrolactamization," <u>J. Org. Chem.</u> , 1990, 55(9), 2786-97.

Examiner

Date Considered:

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.

Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419

Applicant

Ross, et al.

Filing Date
August 14, 1998Group Art Unit
1614**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Sub-Class	Filing Date
GA	4,593,102	6/3/86	Shanklin Jr.			7/1/95
GB	4,578,474	3/25/86	Krapcho et al.			11/19/84

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Sub-Class	Trans-lation
GC	WO9526337	PCT			Yes
GD	WO9524385	PCT			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

GE	Kaczmar, et al., Makromol. Chem., 1976, 177, 1981-9 (German).
GF	Karle, Isabella L. et al., "Coformation of the oxalamide group in retro-bispeptides. Three crystal structures," Int. J. Pept. Protein Res., 1994, 43(2), 160-5.
GG	Kino, Toru et al., "FK-506, A novel immunosuppressant isolated from A streptomyces," J. of Antibiotics, 1987, 40(9), 1249-55.
GH	Kocienski, P. et al., "A synthesis of the C(1)-C(15) segment of tsukubaenolide (FK506)," Tetrahedron Lett., 1988, 29(35), 4481-4.
GI	Krit, N.A. et al., "Impact of the nature of alkyl radical on the biological activity of N-carboxyalkyl dipeptides," Khim.-Farm. Zh., 1991, 25(7), 44-6. (Russian)
GJ	Linde, Robert G. et al., "Straightforward synthesis of 1,2,3-tricarbonyl systems," J. Org. Chem., 1991, 56(7), 2534-8.
GK	Luengo, Juan I. et al., "Efficient removal of pipicolinate from rapamycin and FK506 by reaction with tetrabutylammonium cyanide," Tetrahedron Lett., 1993, 34(29), 4599-602.
GL	Luengo, J. et al., "Studies on the chemistry of rapamycin: novel transformation under Lewis-acid catalysis," Tetrahedron Lett., 1993, 34(6), 991-4.
GM	Luengo, J.I. et al., "Synthesis and Structure-Activity Relationships of Macrocyclic FKBP Ligands," <u>Bioorganic & Medicinal Chemistry Letters</u> , (1994) 4:2, 321-324.
GN	Luengo, J. et al., "Structure-activity studies of rapamycin analogs: evidence that the C-7 methoxy group is part of the effector domain and positioned at the FKBP:12-FRAP interface," Chem. Biol., 1995, 2(7), 471-81.
GO	Lyons, W. Ernest et al., "Neronal Regeneration Enhances the Expression of the Immunophilin FKBP-12," The Journal of Neuroscience, 1995, 15, 2985-94.

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.
 Draw line through citation if not in conformance and not considered.
 Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419

Applicant

Ross, et al.

Filing Date
August 14, 1998Group Art Unit
1614**U.S. PATENT DOCUMENTS**

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	HA	4,574,079	3/4/86	Gavras, H.P. et al.			3/4/86
	HB	4,531,964	7/30/85	Shimano et al.			8/29/83

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub-Class	Trans-lation
	HC	WO9512572	5/11/95	PCT			Yes
	HD	WO9413629	6/23/94	PCT			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	HE	Marshall, J.A. et al., "Convenient synthesis of dioxopiperazines via aminolysis of .alpha.-(pyruvylamino) esters, Synth. Commun., 1975, 5(3), 237-44.
	HF	Mashkovskii, M.D. et al., "1-[4-(2-Hydroxy-3-tert-butylaminopropoxy)-indole-3-yl (5-acetamido-1-(S)-carboxypentyl)-DL-alanyl]-L-proline dihydrochloride, a new angiotensin-converting enzyme inhibitor with β -adrenoblocking properties," Khim.-Farm. Zh., 1993, 27(10), 16-20. (Russian)
	HG	Munegumi, Toratane et al., "Asymmetric Catalytic Hydrogenations of N-pyruvoyl-(S)-proline esters," Bull. Chem. Soc. Jpn., 1987, 60(1), 243-53.
	HH	Munoz, Benito et al., " α -Ketoamide Phe-Pro isostere as a new core structure for the inhibition of HIV protease," Bioorg. Med. Chem., 1994, 2(10), 1085-90.
	HI	Nakatsuka, M et al., "Total Synthesis of FK506 and an FKBP Reagent, (C ₈ , C ₉ - ¹³ C ₂)-FK-506," J. Am. Chem. Soc., 1990, 112(14), 5583-90..
	HJ	Nelson, F. et al., "A novel ring contraction of rapamycin," Tetrahedron Lett., 1994, 35(41), 7557-60.
	HK	Nicolaou, K.C. et al., "Total Synthesis of rapamycin," J. Am. Chem. Soc., 1993, 115(10), 4419-20.
	HL	Pattenden, Gerald and Tankard, Mark, "Facile Synthesis of the tricarbonyl subunit in the immunosuppressant rapamycin," Tetrahedron Lett., 1993, 34(16), 2677-80.
	HM	Ponticelli, Claudio, "Treatment of the Nephrotic Syndrome with Cyclosporin A," J. of Autoimmunity, 1992, 5, 315-24.
	HN	Ranganathan, Darshan et al., "Protein Backbone Modification by Novel C α -C Side-Chain Scission," 1994, J. Am. Chem. Soc., 116(15), 6545-57.

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.
 Draw line through citation if not in conformance and not considered.
 Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419

Applicant

Ross, et al.

Filing Date

August 14, 1998

Group Art Unit

1614

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Sub-Class	Filing Date
	IA	4,390,695	1/28/83	Krapcho et al.			6/1/81
	IB	4,374,829	2/22/83	Harris, E., et al.			2/22/83
	IC	4,310,461	1/12/82	Krapcho et al.			1/23/80
	ID	4,070,361	1/24/78	Petrillo, Jr.			4/21/77

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub-Class	Translation
	IE	WO9407858	4/14/94	PCT			Yes
	IF	WO9405639	3/17/94	PCT			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	IG		Rao, A.V., et al., "Studies directed towards the synthesis of immunosuppressive agent FK-506: construction of the tricarbonyl moiety," Tetrahedron Lett., 1990, 31(10), 1439-42.
	IH		Rao, A.V. Rama et al., "Studies directed towards the synthesis of immunosuppressive agent FK-506: synthesis of the entire bottom half," Tetrahedron Lett., 1991, 32(9), 1251-4.
	II		Rao, A.V. Rama and Desibhatla, Vidyanand, "Studies directed towards the synthesis of rapamycin: stereoselective synthesis of C-1 to C-15 segment," Tetrahedron Lett., 1993, 34(44), 7111-14.
	IJ		Shu, A. et al., "Synthesis of I-125 labeled photoaffinity rapamycin analogs," J. Labelled Compd. Radiopharm., 1996, 38(3), 277-37.
	IK		Skotnicki, Jerauld et al., "Ring expanded rapamycin derivatives," Tetrahedron Lett., 1994, 35(2), 201-2.
	IL		Skotnicki, Jerauld et al., "Synthesis of secorapamycin esters and amides," Tetrah. Lett., 1994, 35(2), 197-200.
	IM		Slee, Deborah H. et al., "Selectivity in the Inhibition of HIV and FIV Protease: Inhibitory and Mechanistic Studies of Pyrrolidine-Containing α -Keto Amide and Hydroxyethylamine Core Structures, J. Am. Chem. Soc., 1995, 117(48), 1187-78.
	IN		Smith, A.B. et al., "Total synthesis of rapamycin and demethoxyrapamycin," J. Am. Chem. Soc., 1995, 117(19), 5407-8.
	IO		Soai, Kenso and Ishizaki, Miyuki, "Diastereoselective asymmetric allylation of chiral α -keto amides with allyltrimethylsilane. Preparation of protected homoallylic alcohols," J. Chem. Soc., 1984, 15, 1016-1017.

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.
 Draw line through citation if not in conformance and not considered.
 Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATION

Attorney Docket 23138S	Serial Number 09/134,419
Applicant Ross, et al.	
Filing Date August 14, 1998	Group Art Unit 1614

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Sub-Class	Filing Date
JA						

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Sub-Class	Translation
JB	WO9325546	12/23/93	PCT			Yes
JC	WO9323548	11/15/93	PCT			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

JE	Soai, Kenso and Hasegawa, Hitoshi, "Diastereoselective reduction of chiral α -ketoamides derived from (S)-proline esters with sodium borohydride. Preparation of optically active α -hydroxy acids," J. Chem. Soc., 1985, 1(4), 769-72.
JD	Soai, Kenso et al., "Asymmetric Allylation of α -keto amides Derived from (S)-proline esters," Pept. Chem., 1986, 24, 327-330.
JF	Soai, Kenso and Ishizaki, Miyuki, "Asymmetric Synthesis of Functionalized tertiary alcohols by diastereoselective allylation of chiral α -keto amides derived from (S)-proline esters: control of stereochemistry based on saturated coordination of Lewis acid," J. Org. Chem., 1986, 57(17) 3290-5. (English)
JG	Soai, Kenso et al., "Asymmetric synthesis of both enantiomers of α -hydroxy acids by the diastereoselective reduction of chiral α -keto amides with complex metal hydrides in the presence of a metal salt," Chem. Lett., 1986, 11, 1897-900.
JH	Steffan, Robert J. et al., "Base catalyzed degradations of rapamycin," Tetrahedron Lett., 1993, 34(23), 3699-702.
JI	Steglich, Wolfgang and Hinze, Sabine, "A rational synthesis of N-trifluoroacetyl amino acids," Synthesis, 1976, 8, 399-401. (German)
JJ	Steglich, Wolfgang et al., "Activated carboxylic acid derivatives. II. A simple synthesis of 2-oxycarboxylic acid amides, N-(2-oxoacyl)amino acid esters and 2-oxocarboxylic acid hydrazides," Synthesis, 1978, 8, 622-4. (German)
JK	Steiner, Joseph P. et al., "High brain densities of the immunophilin FKBP colocalized with calcineurin," Nature Lett., 1992, 358, 584-7.
JL	Steiner, J.P. et al., "Nonimmunosuppressive Ligands for Neuroimmunophilins Promote Nerve Extension <i>In Vitro</i> and <i>In Vivo</i> ," Society for Neuroscience Abstracts, 1996, 22, 297.13.

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.

Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419Applicant
Ross, et al.Filing Date
August 14, 1998Group Art Unit
1614

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Sub-Class	Filing Date
KA						

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Sub-Class	Translation
KB WO9313066	7/8/93	PCT			Yes
KC WO9307269	4/15/93	PCT			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

KD	Stocks, M. et al., "The contribution to the binding of the pyranoside substituents in the excised binding domain of FK-506," Bioorg. Med. Chem. Lett., 1994, 4(12), 1457-60.
KE	Stocks, M. et al., "Macrocyclic ring closures employing the intramolecular Heck reaction," Tetrahedron Lett., 1995, 36(36), 6555-8.
KF	Tanaka, H. et al., "Structure of FK506, a novel immunosuppressant isolated from Streptomyces," J. Am. Chem. Soc., 1987, 109(16), 5031-3.
KG	Tatlock, J. et al., "High affinity FKBP-12 ligands from (R)-(-)-carvone. Synthesis and evaluation of FK506 pyranose ring replacements," Bioorg. Med. Chem. Lett., 1995, 5(21), 2489-94.
KD	Teague, S.J. et al., "Synthesis and Study of a Non-Macrocyclic FK506 Derivative," Bioorg. Med. Chem. Lett., (1994) 4:13, 1581-1584.
KI	Teague, S. et al., "Synthesis of FK506-cyclosporin hybrid macrocycles," Bioorg. Med. Chem. Lett., 1995, 5(20), 2341-6.
KJ	Tindall, Richard S.A., "Immunointervention with Cyclosporin A in autoimmune Neurological Disorders," J. of Autoimmunity, 1992, 5, 301-13.
KK	Tugwell, Peter, "Cyclosporin in the Treatment of Rheumatoid Arthritis," J. of Autoimmunity, 1992, 5, 231-40.
KL	Waldmann, Herbert, "Amino acid esters as chiral auxiliaries in Barbier-type reactions in aqueous solutions," Liebigs Ann. Chem., 1991, (12), 1317-22. (German)
KM	Waldmann, Herbert, "Proline benzyl ester as chiral auxiliary in Barbier-type reactions in aqueous solution," 1990, Synlett, 10, 627-8.
KN	Wang, C.P. et al., "High performance liquid chromatographic isolation and spectroscopic characterization of three major metabolites from the plasma of rats receiving rapamycin (sirolimus) orally," J. Liq. Chromatogr., 1995, 18(13), 2559-68.

Examiner

Date Considered

EXAMINER: Inif reference considered, whether or not citation is in conformance with MPEP § 609.
 Draw line through citation if not in conformance and not considered.
 Include copy of this form with next communication to Applicant.ital

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419

Applicant

Ross, et al.

Filing Date
August 14, 1998Group Art Unit
1614**U.S. PATENT DOCUMENTS**

Examiner Initial	Document Number	Date	Name	Class	Sub-Class	Filing Date
LA						

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Sub-Class	Translation
LB	WO9221313	12/10/92				
LC	WO9219745	11/12/92				

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

LD	Wang, C.P. et al., "A high performance liquid chromatographic method for the determination of rapamycin {sirolimus} in rat serum, plasma, and blood and in monkey serum," J. Liq. Chromatogr., 1995, 18(9), 1801-8.
LE	Wang, G.T. et al., "Synthesis and FKBP Binding of Small Molecule Mimics of the Tricarbonyl Region of FK506, Bioorg. Med. Chem. Lett., (1994) 4:9, 1161-1166.
LF	Wasserman, H.H. et al., " Synthesis of the tricarbonyl region of FK-506 through and amidophosphorane [Erratum to document cited in CA111(7):57366p]," J. Org. Chem., 1989, 54(22), 5406.
LG	Whitesell, J.K. et al., "Asymmetric Induction. Reduction, Nucleophilic Addition to, Ene Reactions of Chiral α -Ketoesters," J. Chem. Soc., Chem Commun., 1983, 802.
LH	Williams, D.R. and Benbow, J.W., "Synthesis of the α,β diketo amide segment of the novel immunosuppressive FK506," J. Org. Chem., 1988, 53(19), 4643-4.
LI	Yohannes, Daniel et al., "Degradation of rapamycin: synthesis of a rapamycin-derived fragment containing the tricarbonyl and triene sectors," Tetrahedron Lett., 1993, 34(13), 2075-8.
LJ	Yamamoto, S. et al., "Stimulation of hair growth by topical application of FK506, a potent immunosuppressive agent," J. Invest. Dermatol., (1994) 102:2, 160-164.

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.
 Draw line through citation if not in conformance and not considered.
 Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE CITATIONAttorney Docket
23138SSerial Number
09/134,419

Applicant

Ross, et al.

Filing Date
August 14, 1998Group Art Unit
1614**U.S. PATENT DOCUMENTS**

Examiner Initial		Document Number	Date	Name	Class	Sub- Class	Filing Date
	MA						
	MB						

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Sub- Class	Trans- lation
	MC	WO9219593	11/12/92	PCT			Yes
	MD	WO9218478	10/29/92	PCT			Yes
	ME	WO9216501	10/1/92	PCT			Yes
	MF	WO9204370	3/19/92	PCT			Yes
	MG	WO9203472	3/5/92	PCT			Yes
	MH	WO9200278	1/9/92	PCT			Yes
	MI	WO9113088	9/5/91	PCT			Yes
	MJ	WO9104985	4/18/91	PCT			Yes
	MK	WO9012805	11/1/90	PCT			Yes
	ML	WO8809789	12/15/88	PCT			Yes
	MM	ZA9207782	4/28/93	South Africa			Yes

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

Examiner

Date Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP § 609.
 Draw line through citation if not in conformance and not considered.
 Include copy of this form with next communication to Applicant.